REMARKS

Upon entry of this amendment, claims 1-56 are currently pending in this application. Claims 23-31 are withdrawn from consideration as allegedly drawn to unelected embodiments. Claims 1-10, 13, 16, 19, and 20-22 are amended to correct minor informalities and to redraft claim 5 in independent form. New claims 32-56 are added. Support for those amendments can be found throughout the specification, *e.g.*, at original claims 1-22, paragraphs [012], [014], [050], [053], [057], [064], and [065], and the Examples. Thus, no new matter has been added.

FORMAL MATTERS

A. Withdrawn Objections and Rejections

Applicant acknowledges, with appreciation, that the Office has withdrawn the following objections and rejections:

- The objection to the specification for using the term "sample" in paragraph [0133];
- The rejection of claims 1-22 under 35 U.S.C. § 112, ¶ 1, as allegedly failing to comply with the written description requirement;
- The rejection of claims 1-22 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite; and
- The rejection of claims 1-3, 7, 9-12, 16, and 17 under 35 U.S.C. § 102(b) as allegedly anticipated by Klein et al.

See Office Action at Item 3 on p. 2.

B. Information Disclosure Statement

Applicant notes that the Image File Wrapper for this application does not contain an initialed copy of the Form SB-08 that was filed April 3, 2002, indicating that the Office has considered all of the documents listed on that form. In a telephonic interview

conducted by Applicant's representative on November 1, 2006, Supervisory Examiner Terry McKelvey confirmed that all of the documents originally submitted on April 3, 2002, had been received and would be considered. Accordingly, Applicant has attached a copy of the Form SB-08 filed April 3, 2002, and respectfully requests that the Examiner indicate that the listed documents were considered by making appropriate notations on the attached form.

REJECTIONS UNDER 35 U.S.C. § 112, ¶ 2

A. Claim 1

Claim 1 is rejected under 35 U.S.C. § 112, ¶ 2 as allegedly indefinite for reciting the phrase "using measurement method 2, wherein measurement method 1 and measurement method 2 are different." *See* Office Action at Item 5 on p. 3. Specifically, the Office contends that "[t]here is no antecedent basis for measurement method 1 or for measurement method 2. Further, it is unclear what measurement methods applicant is referring to." *Id.* Applicant respectfully traverses.

Without acquiescing to the rejection, and solely to facilitate prosecution, claim 1 is amended to replace the phrases "measurement method 1" and "measurement method 2" with the phrases "a first measurement method" and "a second measurement method." Applicant respectfully submits that currently amended claim 1 is definite, and respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 112, ¶ 2.

B. Claim 2

Claim 2 is rejected under 35 U.S.C. § 112, ¶ 2 as allegedly indefinite for reciting the phrases "[t]he method of claim 1" and "wherein the method comprises." *See* Office Action at Item 5 on p. 3. Specifically, the Office contends that "it is unclear if applicant is

referring to measurement method 1, measurement method 2 or the method as recited in the preamble of claim 1." *Id.* Applicant respectfully traverses.

Without acquiescing to the rejection, and solely to facilitate prosecution, claim 2 is amended to recite "[t]he method of claim 1 for detecting an analyte A in a sample." Applicant respectfully submits that currently amended claim 2 is definite, and respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 112, ¶ 2.

C. Claim 5

Claim 5 is rejected under 35 U.S.C. § 112, ¶ 2 as allegedly indefinite for reciting steps (i)-(iii) and the phrase "R3 which is associated with a member X of a specific binding pair." *See* Office Action at Item 5 on p. 3. Regarding steps (i)-(iii), the Office contends that "it is unclear if the steps (i) - (iii) recited in claim 5 replace steps (i) -(ii) recited in claim 1 or if claim 1 further comprises the steps listed in claim 5." *Id.* Regarding the phrase "R3 which is associated with a member X of a specific binding pair," the Office contends that "[i]t is unclear if the R3 associated with L2 recited in claim 1 further comprises a member X or if the R3 or the L2 is considered to be a member X, or if the analyte is a member X because it is a member of a specific binding pair when bound to R3." *Id.* Applicant respectfully traverses.

Without acquiescing to the rejection, and solely to facilitate prosecution, claim 5 is redrafted in independent form and is amended to replace the phrase "a member X of a specific binding pair" with the phrase "a first member of a specific binding pair." Applicant respectfully submits that currently amended claim 5 is definite, and respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 112, ¶ 2.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-15 and 19-22 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,739,042 to Frengen et al. ("*Frengen*") in view of U.S. Patent No. 5,981,180 to Chandler et al. ("*Chandler*"). Specifically, the Office contends that:

- *Frengen's* labeled ligand allegedly reads on "an analyte A-specific binding partner R1, which is associated with a solid phase," and *Frengen's* first and second forms of solid-supported binding partners allegedly read on "an analyte A-specific binding partner R2, which is associated with a label L1" and "an analyte A-specific binding partner R3, which is associated with a label L2," respectively. *See* Office Action at Item 7 on p. 4.

- "Frengen discloses that the solid support (L1 label) associated with a specific binding partner (R2) requires a longer incubation than does the saturation of specific binding partner (R3) (col. 5)." *Id.* at pp. 4-5.

- *Chandler* allegedly establishes that *Frengen* inherently discloses "that the particles . . . are being detected at different time intervals." *Id.* at p. 5.

- *Frengen's* disclosure of the biotin/avidin system "for providing binding to the analyte and also for providing for the indirect detection of the analyte" allegedly reads on the X and Y binding members of the currently pending claims. *Id.*

Applicant respectfully traverses.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (8th Ed., July 2008 Rev.) (citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)). Applicant respectfully submits that *Frengen* cannot anticipate the instant invention because it does not teach each and every element of currently pending claims.

For instance step (i) of independent claims 1, 5, and 19 recites:

> [I]incubating an incubation mixture comprising a sample with an analyte A-specific binding partner R1 . . . an analyte A-specific binding partner R2 . . . and an analyte A-specific binding partner R3.

In contrast, *Frengen* teaches that "the two forms of binding partner are reacted successively rather than simultaneously with the analyte and labeled ligand." *Frengen* at col. 3, ll. 53-55; *see also* col. 4, ll. 1-4 ("the sample is reacted with the first form of solid-supported binding partner and after an appropriate interval with the second form of solid-supported binding partner"); and col. 10, ll. 10-15 ("40 μl of a suspension of MP 6.5 . . . were added. The mixture was incubated for 1 hour . . . wherafter 40 μl of a suspension of MP 7.5 . . . were added"). Thus, *Frengen* teaches that the analyte binding agents are incubated with the sample in at least two separate steps. Accordingly, *Frengen* does not anticipate the currently pending claims, which recite that the analyte binding agents are incubated with the sample in a single step.

In addition, independent claims 1, 5, and 19 recite:

> [B]inding partners R2 and R3 are selected such that saturation of analyte A-binding sites of the binding partner R2 requires a) a higher analyte A concentration, b) a longer incubation, or c) a higher analyte A concentration and a longer incubation, than does saturation of analyte A-binding sites of the binding partner R3.

In contrast, *Frengen* provides no guidance regarding the selection of analyte binding partners based on saturation of their analyte binding sites. The Office cites column 5 of *Frengen* as allegedly teaching that "the solid support (L1 label) associated with a specific binding partner (R2) requires a longer incubation than does the saturation of specific binding partner (R3)." Office Action at pp. 4-5. Applicant has reviewed column

5 of *Frengen* and respectfully submits that it contains no teaching regarding the selection of anayte binding partners based on the concentration or incubation time required to saturate their analyte binding sites, as required by the currently pending claims. Applicant assumes the Office is referring to the following statements in column 5 of *Frengen*:

> The time interval between reaction with the first and second forms of solid-supported binding partner is not critical provided that it is kept substantially constant for a given assay system.
>
> . . .
>
> Since addition of the second form of solid-supported binding partner . . . effectively quenches reaction of the analyte with the first form of solid-supported biding partner, the process of the invention avoids any need to allow the first form of solid supported binding partner to reach equilibrium with the analyte.

Frengen at col. 5, ll. 7-10 and 14-20. However, these statements do not teach that the selection of analyte binding partners should be based on saturation of their analyte binding sites, as required by claims 1, 5, and 19. Accordingly, *Frengen* does not anticipate the currently pending claims.

Moreover, independent claims 1, 5, and 19 recite:

> [D]etermining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 and time T2 are different.

In contrast, *Frengen* teaches "[p]article-associated light scatter and fluorescence signals were measured simultaneously and registered as correlated two-parameter histograms." *Frengen* at col. 10, ll. 25-27; *see also* col. 10, ll. 33-35 ("The simultaneously-measured standard curves for MP 6.5 (p1) particles and MP 7.5 (p2)

particles . . . are shown in FIG. 2A"). Thus, *Frengen* teaches that the measurement signals are determined at the same time, not at different times, as required by claims 1, 5, and 19. Accordingly, *Frengen* does not anticipate the currently pending claims.

The Office contends, however, that since "Frengen teaches that the independently determinable forms of solid support binding partners bound with the analyte and labeled ligand are determined by flow cytometry in a gated manner," and *Chandler* allegedly teaches that "flow cytometry requires a fluid suspension of particles in a flow down a stream in single file and passed through a examination zone in this manner to detect the individual particles," then "it is inherent that the particles of Frengen are being detected at different time intervals." Office Action at Item 7 on p. 5. Nevertheless, *Frengen's* use of flow cytometry does not establish that the measurement signals are determined at different times, as required by the currently pending claims. In fact, as discussed above, *Frengen* teaches that the measurement signals determined therein, *i.e.*, particle-associated light scatter and fluorescence signals, were measured simultaneously. Thus, although *Frengen's* particles may pass through the examination zone individually, the measurement signals are determined at the same time. Accordingly, *Frengen* does not anticipate the currently pending claims, which require that the measurement signals are determined at different times.

Chandler fails to cure the deficiencies in *Frengen*, because *Chandler* does not establish that *Frengen* inherently teaches: (1) incubating the analyte binding agents with the sample in a single step; (2) selecting the analyte binding partners based on saturation of their analyte binding sites; and (3) determining the various measurement signals at different times. For at least these reasons, Applicant submits that *Frengen*

does not anticipate claims 1-15 and 19-22, and respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 102(b).

REJECTIONS UNDER 35 U.S.C. § 103

Claims 16 and 17 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Frengen* in view of Buranda T. et al., "Peptides, Antibodies, and FRET on Beads in Flow Cytometry: A Model System Using Fluoresceinated and Biotinyolated β-Endorphin," Cytometry, 37:21-31 (1999) ("*Buranda*"). *See* Office Action at Item 11. Specifically, the Office acknowledges that "Frengen differs from the instant invention in failing to teach detection by energy transfer," but contends that *Buranda* cures these deficiencies in *Frengen* by allegedly teaching "that it is known in the art of flow cytometry to incorporate fluorescence resonance energy transfer (FRET)." *Id.* Applicant respectfully traverses.

The Office must make several basic factual inquiries to determine whether the claims of a patent application are obvious under 35 U.S.C. § 103. These factual inquiries, set forth in *Graham v. John Deere*, require the Examiner to:

> (1) Determine the scope and content of the prior art;
>
> (2) Ascertain the differences between the prior art and the claims in issue;
>
> (3) Resolve the level of ordinary skill in the pertinent art; and
>
> (4) Evaluate evidence of secondary considerations.

See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966). Once the findings of fact are articulated, the Office "must then make a determination whether the claimed invention 'as a whole' would have been obvious at the time to that person." M.P.E.P. § 2142, 8th

Ed., July 2008 Rev.; *see also KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1734 (2007).

As discussed above, *Frengen* fails to anticipate the invention of claim 1, from which claims 16 and 17 depend, because it does not teach: (1) incubating the analyte binding agents with the sample in a single step; (2) selecting the analyte binding partners based on saturation of analyte binding sites; and (3) determining the various measurement signals at different times. Nothing in *Buranda* establishes that these differences between *Frengen* and the instant invention would have been obvious to a person skilled in the art at the time this invention was made, since *Buranda* merely discloses the use of energy transfer in flow cytometry assays.

For at least these reasons, Applicant respectfully submits that the Office has failed to establish a *prima facie* case of obviousness of claims 16 and 17, and requests that the Office withdraw this rejection under 35 U.S.C. § 103.

B. Claims 16 and 18

Claims 16 and 18 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Frengen* in view of Ullman E.F.. et al., "Luminescent Oxygen Channeling Immunoassay: Measurement of Particle Binding Kinetics by Chemiluminescence," PNAS, 91:5426-30 (1994) ("*Ullman*"). *See* Office Action at Item 12. Specifically, the Office acknowledges that "Frengen differs from the instant invention in failing to teach photosensitizers and chemiluminescent substances," but contends that *Ullman* cures these deficiencies in *Frengen* by allegedly teaching "particles comprising photosensitizers and chemiluminescent substances utilized in luminescent oxygen channeling immunoassays." *Id.* Applicant respectfully traverses.

The legal requirements for establishing obviousness under 35 U.S.C. § 103 are set forth above. As discussed above, *Frengen* fails to anticipate the invention of claim 1, from which claims 16 and 18 depend, because it does not teach: (1) incubating the analyte binding agents with the sample in a single step; (2) selecting the analyte binding partners based on saturation of analyte binding sites; and (3) determining the various measurement signals at different times. Nothing in *Ullman* establishes that these differences between *Frengen* and the instant invention would have been obvious to a person skilled in the art at the time this invention was made, since *Ullman* merely discloses the use of chemiluminescent substances in flow cytometry assays.

For at least these reasons, Applicant respectfully submits that the Office has failed to establish a *prima facie* case of obviousness of claims 16 and 18, and respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 103.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 27, 2009

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Attachments: A copy of the Form SB-08 filed April 3, 2002